

INFECTION S CAUSING ANEMIA

LIST OF MICROORGANISMS CAUSING ANEMIA

Iron deficiency anemia

It occurs due to blood loss, which occurs as a result of infection with various agents, leading to microcytic hypochromic anemia.

- ☐ Hookworm (*Necator americanus* and *Ancylostoma duodenale*)
- ☐ *Trichuris trichiura*
- ☐ *Schistosoma* species

Hemolytic anemia

It occurs due to destruction of RBCs. The various infectious agents include:

- ☐ Malaria (*Plasmodium falciparum*)
- ☐ *Babesia microti*
- ☐ *Bartonella bacilliformis*
- ☐ Clostridial sepsis (*Clostridium perfringens*)
- ☐ Infectious mononucleosis (Epstein-Barr virus)
- ☐ Hepatitis A virus

LIST OF MICROORGANISMS CAUSING ANEMIA (CONT..)

Megaloblastic anemia

- It is caused by a parasite, *Diphyllobothrium latum*
- It causes dissociation of *vitamin B₁₂-intrinsic factor complex* within the gut lumen, which leads to decreased absorption of vitamin B₁₂ in ileum.

Aplastic anemia

Aplastic anemia occurs as a result of bone marrow dysfunction (or failure) leading to a normocytic normochromic type of anemia. This can occur due to infection with various agents such as:

- *M.tuberculosis* , Rickettsial infections
- *Leishmania donovani* , Cytomegalovirus (CMV)
- Epstein-Barr virus , Varicella-zoster virus
- Parvovirus B19 (aplastic crisis in patients with chronic hemolytic anemia)
- Human immunodeficiency virus (HIV) , Human herpesvirus 6 (HHV-6)
- Hepatitis C virus

IRON DEFICIENCY ANEMIA

■ It **occurs due to blood loss**, which occurs as a result of infection with various agents, *leading to microcytic hypochromic anemia*

□ Hookworm (*Necator americanus* and *Ancylostoma duodenale*)

□ *Trichuris trichiura*

□ *Schistosoma* species

HOOKWORM INFECTION

- Hookworm - one of the important causes of iron deficiency anemia in both tropics and temperate countries
- It is one of the soil-transmitted helminths

CLASSIFICATION

- *Ancylostoma duodenale* or old world hookworm
- *Necator americanus* or new world hookworm or American hookworm
- There are several animal parasites that rarely infect man, cause cutaneous larva migrans—*Ancylostoma braziliensis*, *A. caninum* and *A. ceylanicum*

EPIDEMIOLOGY

■ **World:** Hookworm infection is widespread.

- *Necator* infection (835 million) is more common than *Ancylostoma* (135 million)

■ **India:** Hookworm infection is widely prevalent in India.

- *N. americanus* - predominant in South India and *A. duodenale* - North India
- Heavily infected areas are: Assam (tea gardens), West Bengal, Bihar, Odisha, Andhra Pradesh, Tamil Nadu, Kerala and Maharashtra.

EPIDEMIOLOGY (CONT..)

- **Age and sex distribution:** Males and young adults - commonly affected - anemia due to iron loss - more severe in children and pregnant women
- **Endemic index:** *Chandler's index* - used in the epidemiological studies of hookworm disease to estimate the morbidity and mortality in the community due to hookworm infection (which depends much upon the worm

MORPHOLOGY

- Hookworm has three morphological forms: adult, larvae (four stages) and egg
- ***Ancylostoma*** and *Necator* - differentiated by the morphology of adult worm and third stage larva

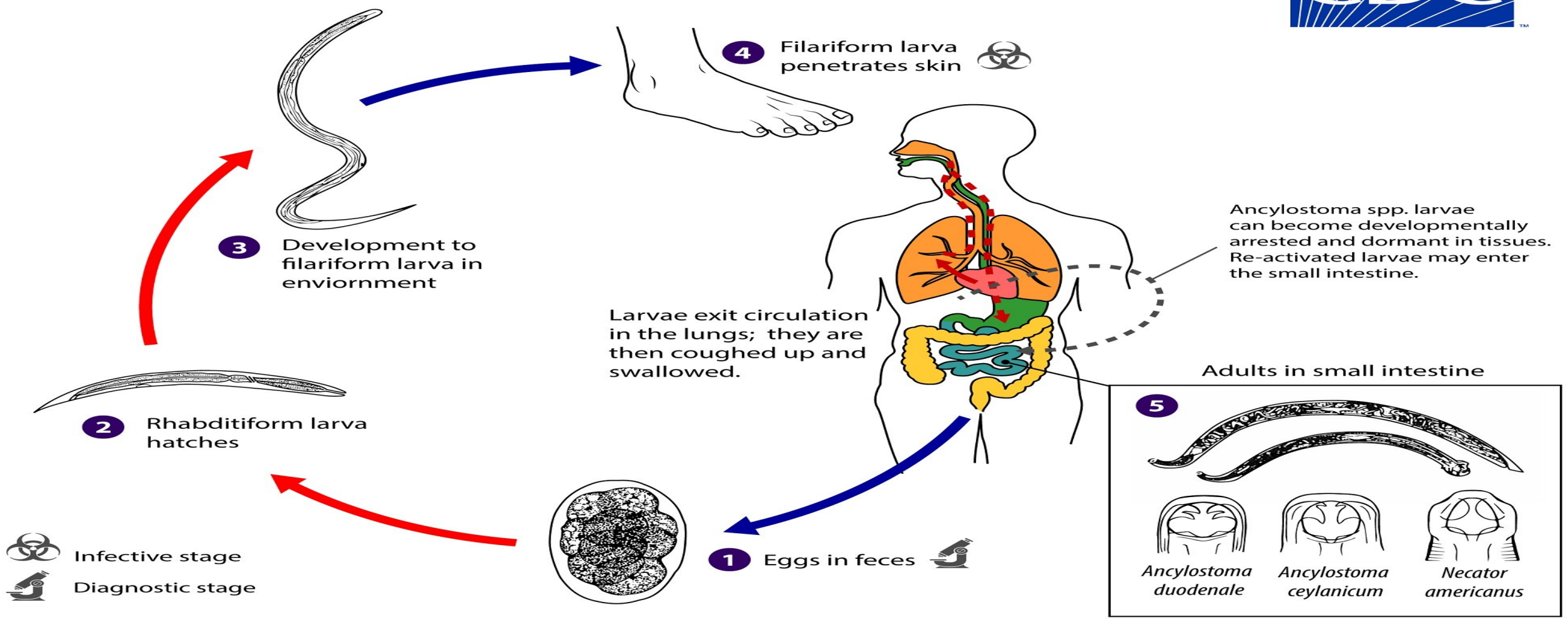
MORPHOLOGY (CONT..)

- Adult worm is small (7–13 mm) in size, has a bent in the anterior end (hence called as hookworm)
- The adult worm of *Ancylostoma* and *Necator* - differentiated by buccal capsule with teeth or cutting plate (present in the anterior end) and copulatory bursa (present in the posterior end)
- *L1 larva* - called as **rhabditiform larva** whereas *L3 stage larva* - called as **filariiform larva**

LIFE CYCLE



Intestinal Hookworm



PATHOGENICITY

Hookworm **has ability to suck blood from the intestinal vessels**, which occurs by several ways:

- Attaching and making cuts in the intestinal wall by buccal capsule and teeth followed by sucking the blood through contraction of their muscular esophagus
- Secreting hydrolytic enzymes
- Releasing anticoagulants – maintain continuous oozing of blood from the attachment site.

CLINICAL FEATURES - *AFFECT DUE TO MIGRATING LARVA*

■ **Cutaneous lesions**

- **Ground itch** - at the site of skin penetration
- **Serpiginous tracks**

■ **Mild transient pneumonitis**

CLINICAL FEATURES - *AFFECT DUE TO ADULT WORM IN INTESTINE*

- Asymptomatic
- Early intestinal phase (less worm load)
- Late intestinal phase (chronic infection with heavy worm load)

LABORATORY DIAGNOSIS - *STOOL MICROSCOPY*

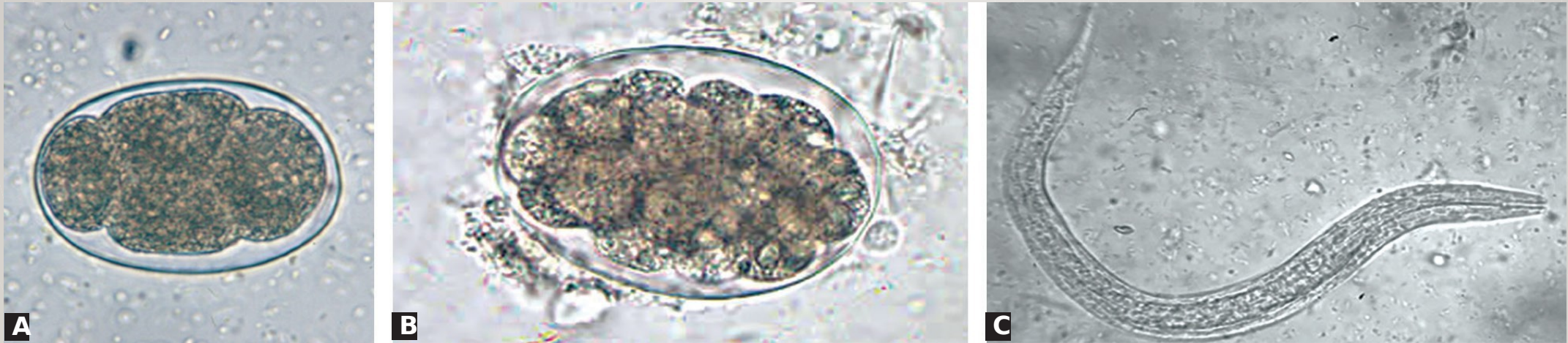
- Stool concentration procedures - required to detect lighter infections

- In a stool sample that is not fresh, the eggs may hatch out to release **rhabditiform larvae**

(1 larva)



LABORATORY DIAGNOSIS - *STOOL MICROSCOPY*



A. Egg with four blastomeres; **B.** Egg with many blastomeres; **C.** Rhabditiform larva.

LABORATORY DIAGNOSIS - *STOOL CULTURE*

- Freshly passed stool samples - cultured - eggs hatch out to develop to L3 stage filariform larvae in 5–7 days - differentiate *A. duodenale* from *N. americanus*
- Various culture techniques used are:
 - Harada-Mori filter paper tube method
 - Baermann funnel technique
 - Charcoal culture method
 - Agar plate technique (more sensitive)

LABORATORY DIAGNOSIS - *MOLECULAR DIAGNOSIS*

- PCR and real-time PCR – developed targeting genes - mitochondrial cytochrome oxidase genes.

Molecular methods have the advantages such as:

- Species specific; can differentiate between *Ancylostoma* and *Necator*
- More sensitive, can detect as low as one copy per 200 mg of stool.

LABORATORY DIAGNOSIS - *OTHER FINDINGS*

- (i) hypochromic microcytic anemia,
- (ii) eosinophilia, and
- (iii) hypoalbuminemia

TREATMENT OF HOOKWORM DISEASE

Antiparasitic:

- Antiparasitic drugs - **albendazole (400 mg once)** or mebendazole (500 mg once) or pyrantel pamoate (11 mg/kg for 3 days) can be given

TREATMENT OF HOOKWORM DISEASE (CONT..)

Symptomatic treatment:

- Mild iron-deficiency anemia - treated with oral iron and folic acid
- Severe hookworm disease with protein loss and malabsorption - nutritional support and oral or parenteral iron replacement

PREVENTION

- Improved personal hygiene
- Proper disposal of feces
- Improved nutrition with dietary iron
- Treatment of infected persons

SOIL-TRANSMITTED HELMINTH INFECTION

- intestinal worms infecting humans
- transmitted through contaminated soil - ***Ascaris, Trichuris and hookworm***

SOIL-TRANSMITTED HELMINTH INFECTION (CONT..)

- **High-risk group** - preschool children, school-age children, women of childbearing age (including pregnant women) and adults in certain high-risk occupations - tea-pickers or miners
- **Presentation:** Infected children - nutritionally, intellectually and physically impaired - suffer from malabsorption of nutrients, anemia, diarrhea and dysentery - depending upon the type of helminths infected

SOIL-TRANSMITTED HELMINTH INFECTION (CONT..)

■ **Deworming:** Periodic prophylactic measure to prevent high-risk people from worm infestation; initiated by World Health Organization (WHO)

- **The National Deworming Day:** Every year, 10th February and 10th August
- Deworming - once in a year if the prevalence of STH infection is >20% in the community and twice a year if >50%

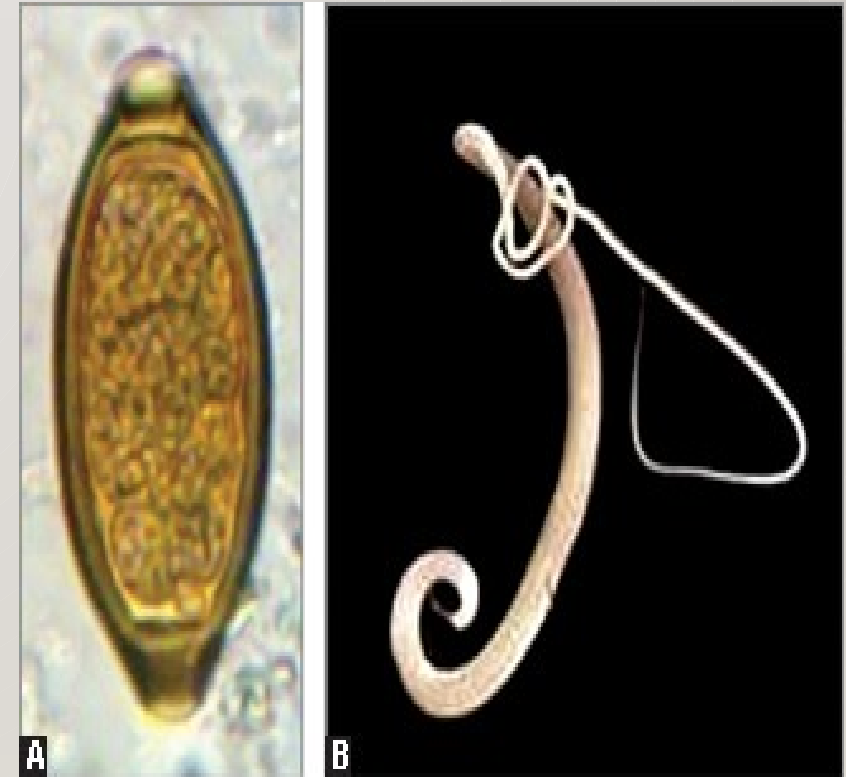
- In this day, single-dose albendazole (400 mg) - all children aged 1-10 years

SOIL-TRANSMITTED HELMINTH INFECTION (CONT..)

- **Elimination:** WHO aim is to eliminate the morbidity due to STH infection in children by 2030
- The global target is kept as $<2\%$ of children have STH infections of moderate and heavy intensity by 2030

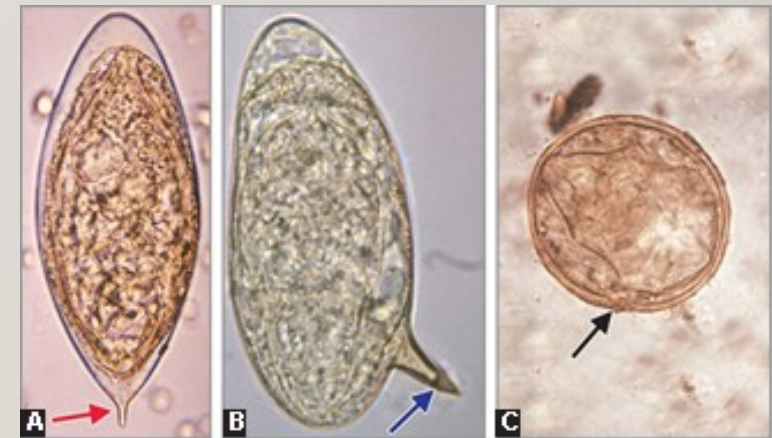
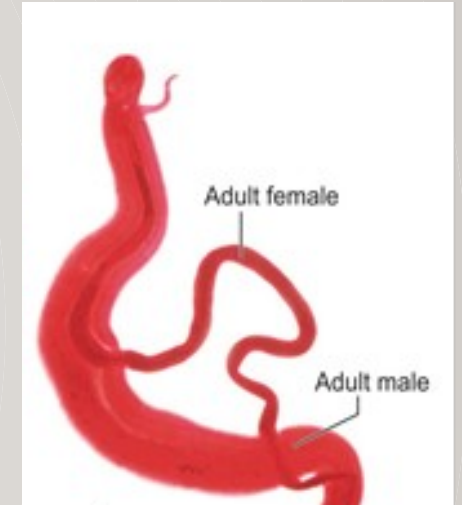
TRICHURIS TRICHURA

- Also known as **whipworm** infection
- Adult female worms get buried in the large intestinal mucosa (Iron deficiency anemia)
- Treatment: Mebendazole (500 mg once) or albendazole (400 mg daily for



SCHISTOSOMA SPECIES

- Schistosomes - known as **blood flukes**
- *S. mansoni* and *S. japonicum*—reside in mesenteric venous plexus (of GIT), cause various GI symptoms
- *S. haematobium* - resides in venous plexus of bladder and causes urinary schistosomiasis and carcinoma of bladder
- **Praziquantel** - drug of choice



Hemolytic anemia

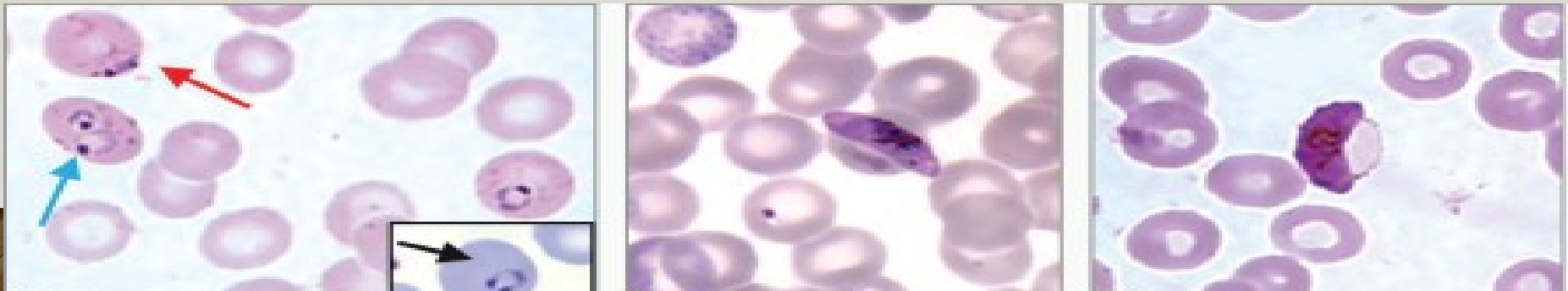
■ It occurs due to **destruction of RBCs**

■ The various infectious agents include:

- Malaria (*Plasmodium falciparum*)
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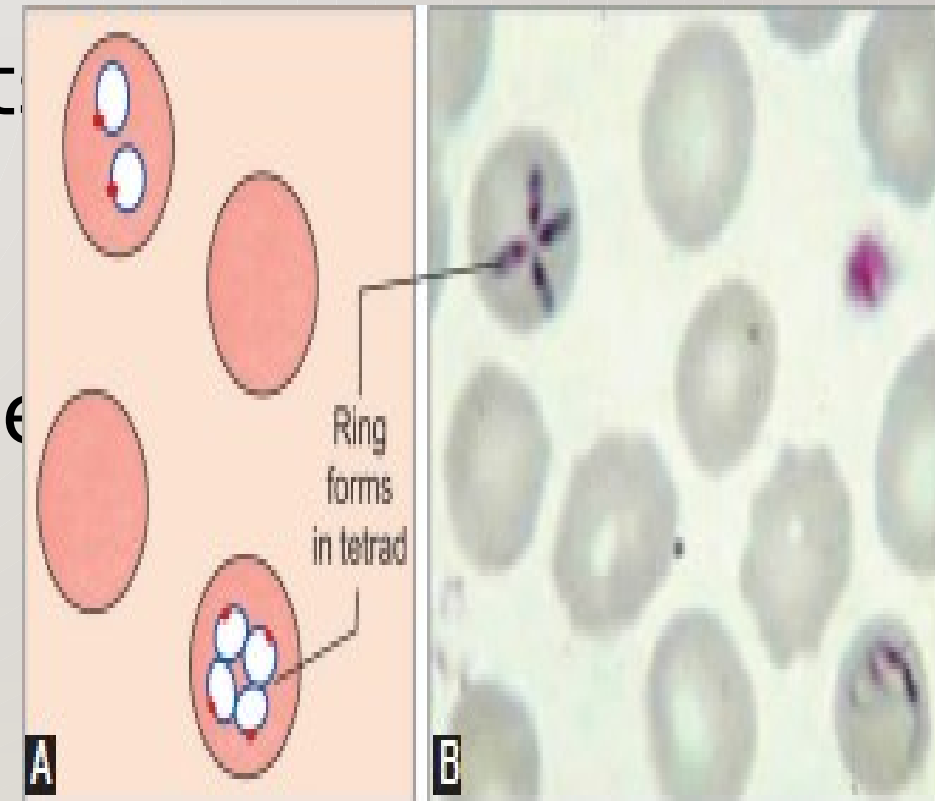
Malaria (*Plasmodium falciparum*)

- Causative agents: *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale* & *P. knowlesi*
- Clinical features: Fever, Anemia, Splenomegaly
- Treatment: Co-formulated tablet of **Artemether and lumefantrine** for 3 days *plus* **Primaquine** (0.75 mg/kg) single dose on second day



Babesia microti

- It is similar to malaria parasite in its life cycle and pathogenesis
- **Hard tick** (*Ixodes scapularis*) is the primary vector (definitive host) of the parasite
- Atovaquone plus azithromycin is given for treatment



BARTONELLOSIS

- Fastidious, facultative intracellular, **gram-negative bacteria**
- Ability to invade mammalian cells and RBCs
- Three important human pathogens: *B.henselae*, *B.quintana* and *B.bacilliformis*.

BARTONELLOSIS (CONT..)

B. henselae

Transmitted by **exposure to cats** (by scratch or bite)

- **Cat-scratch disease** (regional lymphadenopathy and painless papule at the site of scratch)
- **Bacillary angiomatosis** (neovascular lesions involving skin and other organs)
- **Bacillary peliosis** (Angioproliferative disorder involving liver and spleen)

BARTONELLOSIS (CONT..)

B. quintana

Transmitted by louse

- **Trench fever** - mild febrile illness (lasts for 5 days & subsequent episodes occurring every 5-day - 5 days fever).
- **Bacillary angiomatosis**
- **Chronic bacteremia**
- **Endocarditis**

BARTONELLOSIS (CONT..)

B. bacilliformis

Transmitted by vector sandfly (*Lutzomyia*)

■ It produces a biphasic disease:

- Oroya fever or Carrion's disease
- Verruga peruana
- Others - Bacteremia and endocarditis

LABORATORY DIAGNOSIS OF BARTONELLA INFECTIONS

- **Specimens** - Blood, lymph node or skin biopsies
- **Microscopy:** Warthin-Starry silver nitrate staining and immunofluorescence staining - detect *B. henselae* from lymph node smears
- **Culture:** *Bartonella* can be grown on blood agar at 37°C and incubated for 12–15 days

LABORATORY DIAGNOSIS OF BARTONELLA INFECTIONS (CONT..)

- **Antibody detection:** Both indirect immunofluorescence assay (IFA) and enzyme immunoassay (EIA) based methods are available
- **PCR:** Done to amplify the genes such as 16S rRNA gene.

TREATMENT OF BARTONELLOSIS

■ **Cat-scratch disease:**

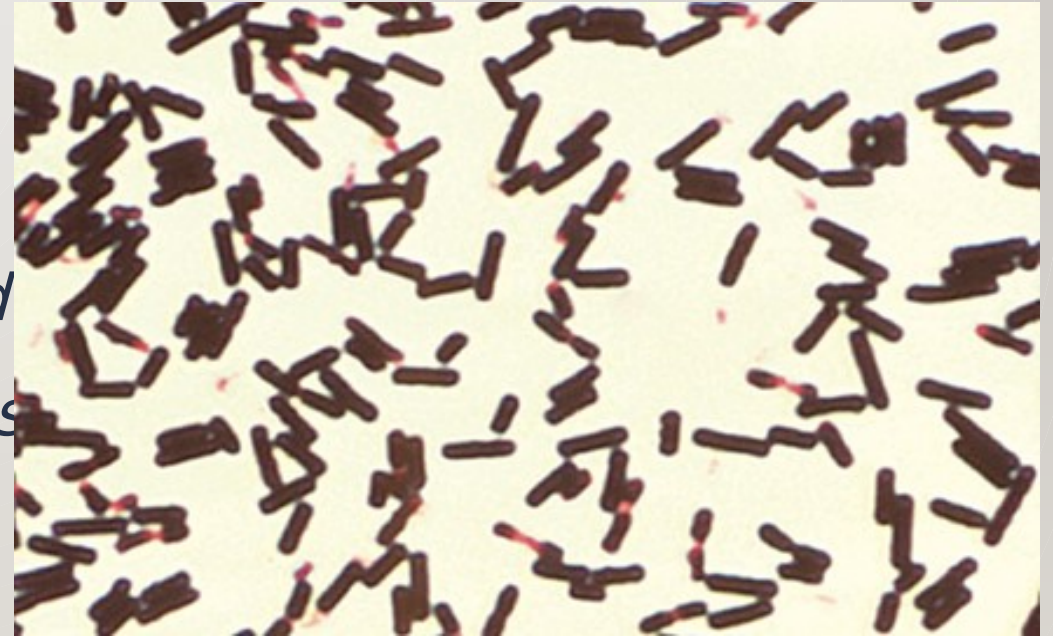
- Treatment - not routinely indicated;
- For extensive lymphadenopathy - azithromycin - 5 days

■ **Bacillary angiomatosis:**

- Erythromycin or doxycycline - 3 months

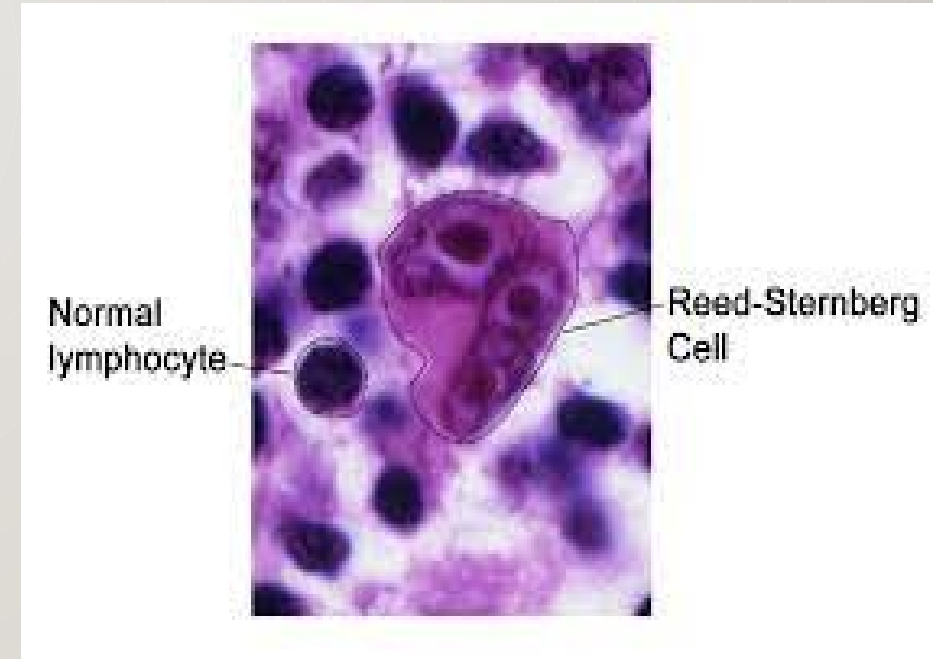
Clostridial sepsis (*Clostridium perfringens*)

- Gram-positive bacillus (**subterminal bulging spores**)
- *Clinical manifestations: Clostridial Wound Infection, Clostridial Enteric Infection, Gas gangrene*
- Combination of penicillin and clindamycin is recommended for 10–14 days



Infectious mononucleosis (Epstein-Barr virus)

- Fever, sore throat, lymphadenopathy, splenomegaly
- Diagnosis:
 - 50 % lymphocytosis with $> 10\%$ Atypical lymphocytes on peripheral blood



Positive Paul Bunnell test

Hepatitis A virus

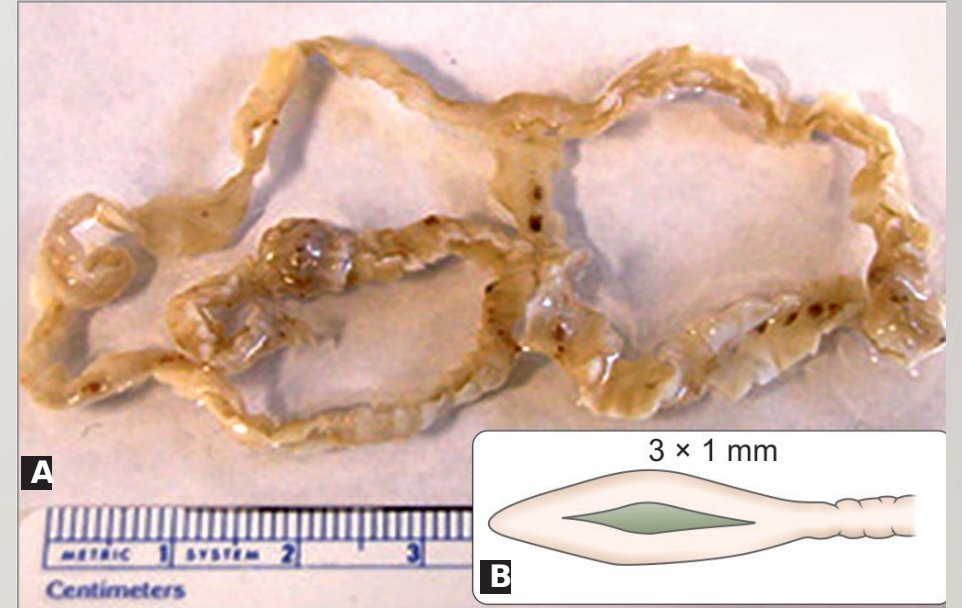
- Transmission: Fecal-oral route or Ingestion of contaminated food or water - raw or undercooked food and ice or frozen foods
- Treatment: Mainly supportive
- **Vaccine-preventable**

DIPHYLLOBOOTHRIASIS

- Diphyllorbothriasis - intestinal parasitic infection, caused by a cestode *Diphyllorbothrium latum*, also known as **fish tapeworm**
- Largest known parasite found in human intestine

MORPHOLOGY

- *D. latum* has three morphological forms:
- 1. **Adult worm**
- 2. **Operculated egg**
- 3. **Larvae:** Three stages - first stage (coracidium), second stage (procercoid larva) and third stage (plerocercoid larva)

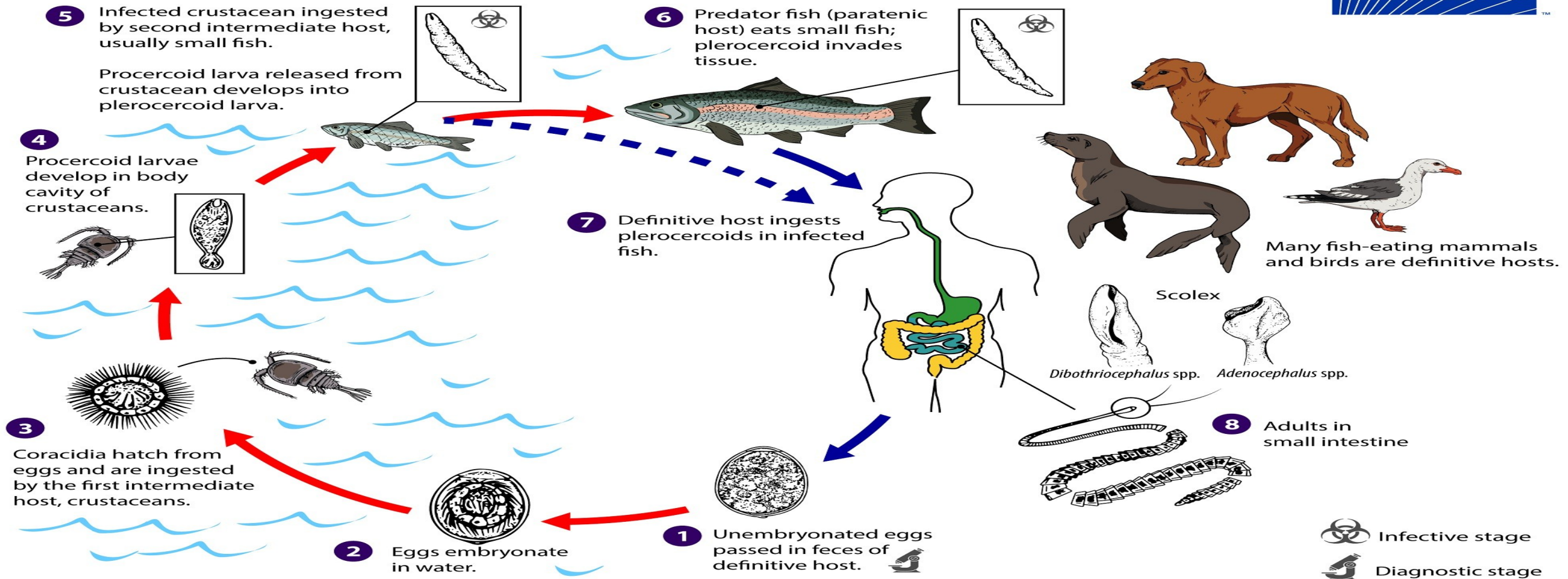


A. Section of an adult worm containing many proglottids; **B.** Scolex (schematic) with two bothria (or grooves).

LIFE CYCLE

4DPDx

Diphyllobothriid Tapeworms



CLINICAL FEATURES

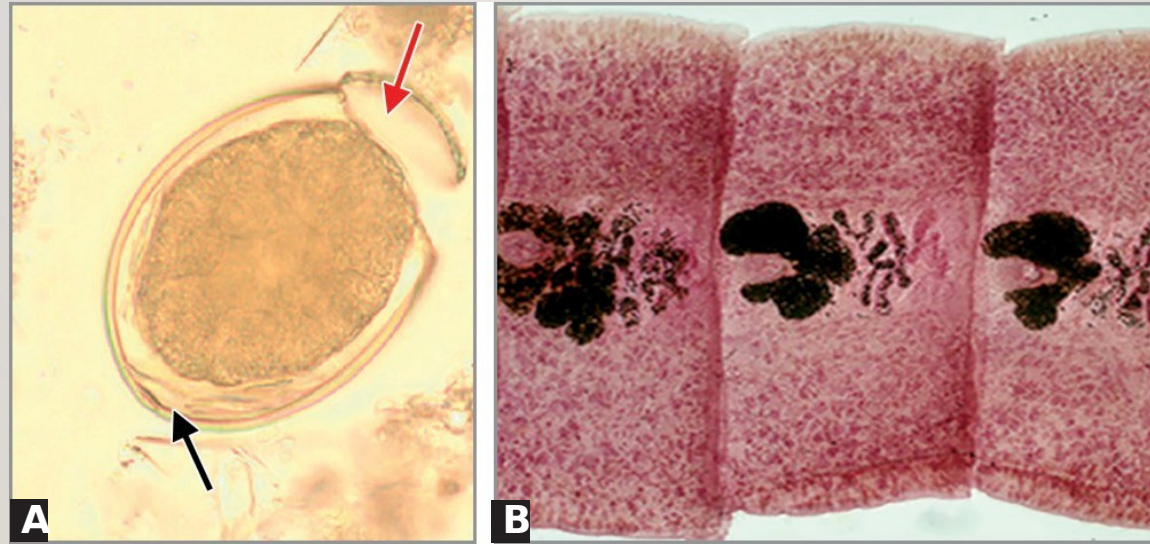
- Most of *D. latum* infections are asymptomatic
- Few individuals develop symptoms
- **Minor manifestations** – abdominal discomfort, diarrhea, vomiting, weakness and weight loss or rarely acute abdominal pain due to intestinal obstruction, cholangitis or cholecystitis

CLINICAL FEATURES (CONT..)

- **Vitamin B12 deficiency:** The adult worm causes dissociation of the vitamin B12-intrinsic factor complex within the gut lumen - leads to a decrease in absorption of B12 at ileum
- Vitamin B12 deficiency leads to development of **megaloblastic anemia** and some people may exhibit neurologic sequelae like paresthesia

LABORATORY DIAGNOSIS

- **Stool examination** - Characteristic eggs and sometime segments of



A. Egg—note the operculum (red arrow) and posterior knob (black arrow); **B** Carmine-stained gravid proglottids—note broader than longer, rosette-shaped ovaries).

LABORATORY DIAGNOSIS (CONT..)

- **Molecular method:** PCR followed by sequencing

- **Blood examination** - eosinophilia and evidence of megaloblastic anemia such as:

- ↑ Mean corpuscular volume and mean corpuscular hemoglobin
- Normal mean corpuscular hemoglobin concentration
- Macrocytes (enlarged RBCs).

TREATMENT OF DIPHYLLOBOTHRIASIS

- Praziquantel (5–10 mg/kg once) - highly effective (drug of choice)
- Niclosamide - given alternatively
- Parenteral vitamin B12 - given if B12 deficiency is manifested

PREVENTION

- Preventive measures - thorough cooking of fish or freezing
- *D. latum* infection - called the **Jewish housewives' disease**, as they acquire infection by tasting the uncooked fish while preparing
- Proper cooking of fish (5 minutes at 55°C)
- Deep freezing (–20°C for 7 days, or –35°C for 15 hours) of fish should be followed for people who eat raw fish.

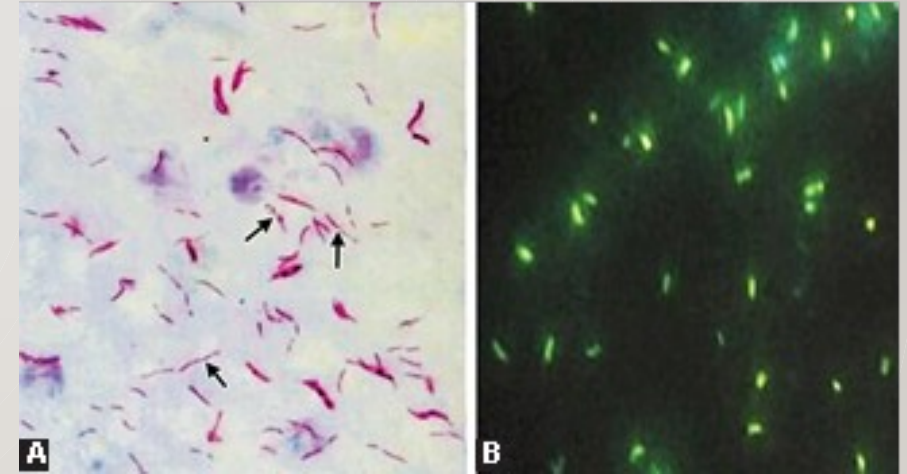
Aplastic anemia

Aplastic anemia occurs as a **result of bone marrow dysfunction (or failure)** leading to a **normocytic normochromic type of anemia**. This can occur due to infection with various agents such as:

- *M.tuberculosis* , Rickettsial infections
- *Leishmania donovani* , Cytomegalovirus (CMV)
- Epstein-Barr virus , Varicella-zoster virus
- Parvovirus B19 (aplastic crisis in patients with chronic hemolytic anemia)
- Human immunodeficiency virus (HIV) , Human herpesvirus 6 (HHV-6)

M. tuberculosis

- Ziehl-Neelsen (ZN) technique
 - long slender, beaded, less uniformly stained red color
 - acid-fast bacilli



- Lowenstein Jensen (LJ)
 - medium—shows rough, tough and buff colored colonies in

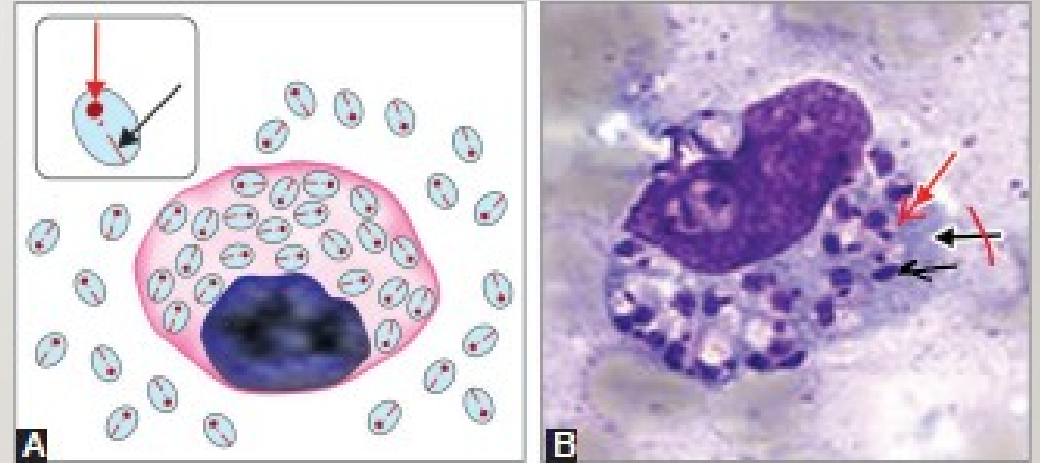


Rickettsial infections

- Small non-motile gram-negative coccobacilli
- Obligate intracellular organisms
- Not cultivable in artificial media (grow in cell lines/by animal & egg inoculation)
- Non-specific test: **Weil-Felix test**; Specific antibody detection—by Indirect IF, ELISA and Indirect

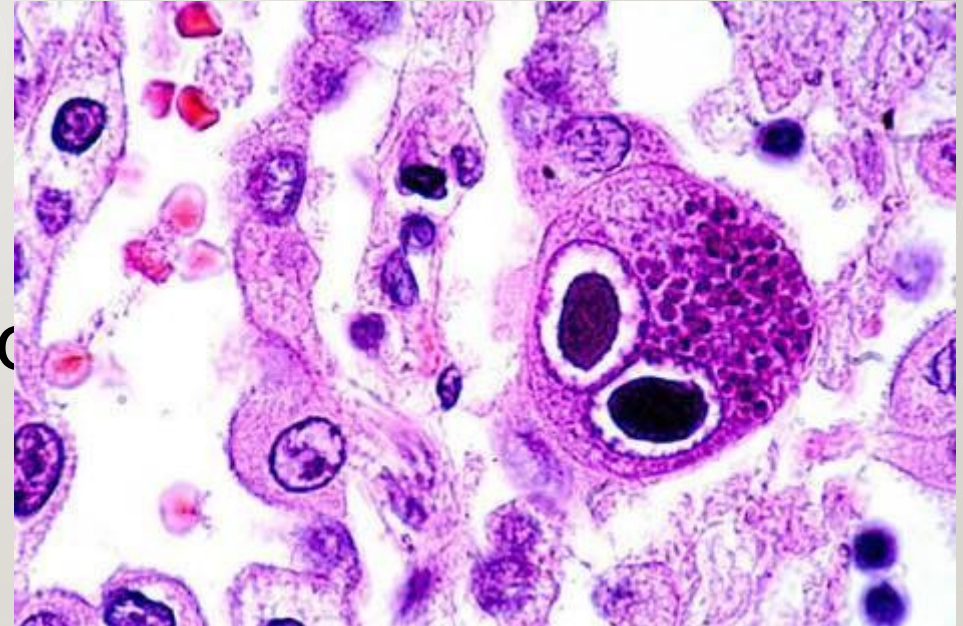
Leishmania donovani

- Obligatory intracellular protozoa; **Vector** - bite of the female sandfly vector
- The various drugs used in the treatment of VL are:
 - (i) Pentavalent antimonials,
 - (ii) Liposomal amphotericin B,
 - (iii) Miltefosine,
 - (iv) Paromomycin



Cytomegalovirus (CMV)

- Owl eye appearance
- Treatment: Ganciclovir, Valganciclovir



Varicella-zoster virus

- Produces vesicular eruptions (rashes) on the skin and mucous membranes in the form of two clinical entities

- **Chicken pox**
- **Zoster or Shingles**



PARVOVIRUS INFECTIONS

- Responsible for - childhood exanthema - **erythema infectiosum (fifth disease)**.
- ***Smallest viruses***
- Non-enveloped with icosahedral symmetry
- **Only DNA viruses - possess single-stranded DNA**

PATHOGENESIS

- **Transmission** - Respiratory route, followed by blood transfusion and transplacental route
- **Infects precursors of RBCs:** Parvovirus B19 has a special tropism for **erythroid progenitor cells present in adult bone marrow** and fetal liver as it binds to blood group P antigen as receptors; which are present on the RBC surface
- This results in **red cell destruction and inhibition of**

CLINICAL MANIFESTATIONS

- Erythema infectiosum (or fifth disease)
- Transient aplastic crisis
- Pure red cell aplasia
- Non-immune hydrops fetalis
- Papular-purpuric gloves and socks syndrome



Fifth disease or rashes with slapped cheek appearance

LABORATORY DIAGNOSIS

Molecular methods:

- PCR - detects viral DNA (e.g. genes coding for VP1 and VP2) from serum, tissue or respiratory secretions
- Real time PCR - used for quantification of viral load in blood, during acute infections

LABORATORY DIAGNOSIS (CONT..)

- **Antibody detection:** ELISA – detecting antibodies against VP1 and VP2 antigens. IgM appears early - recent infection and remains elevated for 2–3 months
- **Antigen detection:** Immunohistochemistry - detect viral antigens in fetal tissues and bone marrow.

TREATMENT OF PARVOVIRUS INFECTIONS

- No antiviral drug is available
- Symptomatic treatment is given
- Immunoglobulins containing neutralizing antibodies to human parvovirus are available commercially

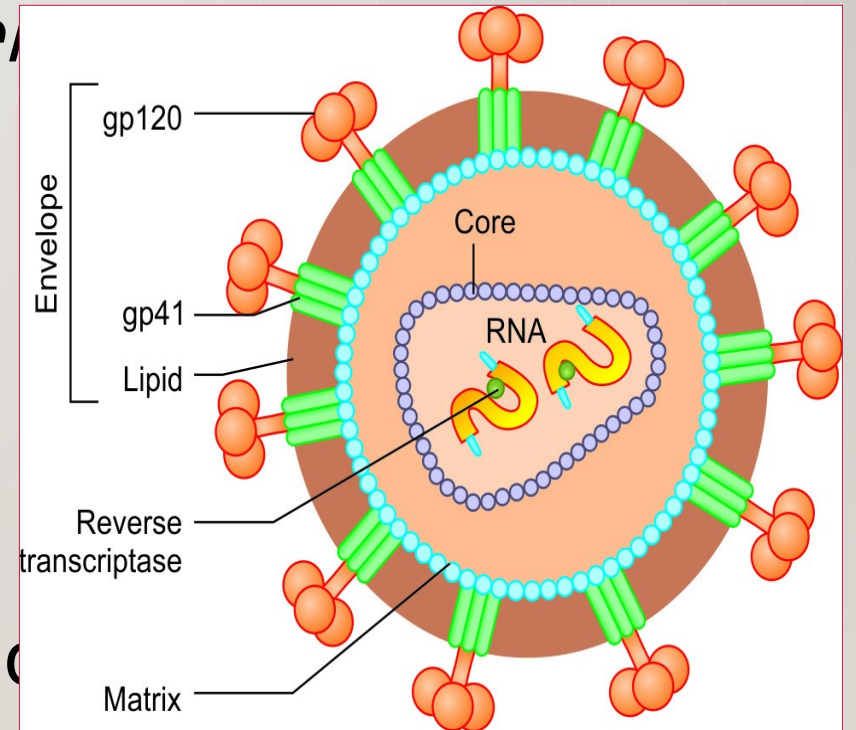
Human immunodeficiency virus (HIV)

- Three structural genes—*gag*, *pol*, and *env*
- Six non-structural or regulatory genes

- **Specific Tests for HIV Infection:**

- Screening tests (antibody detection)
- Supplemental tests (antibody detection)
- Confirmatory tests

- **Non-specific Immunological Methods**



Human herpesvirus 6 (HHV-6)

Transmission - through infected oral secretions

- **Sixth disease:** In children - causes sixth disease – *exanthema subitum* or *roseola infantum* - characterized by high grade fever and skin rashes
- In older age groups - associated with mononucleosis-like syndrome

Hepatitis C virus

- **Parenteral:** Most commonly transmitted through exposure to infectious blood.
- **Vertical transmission** from infected mother to fetus may occur but at much lower rate (6%) than that of HBV (20%)
- **Sexual transmission** (rare).
- Hepatitis C virus **does not spread** through breast milk, food or casual contacts including hugging or kissing
- ELISA is the most common platform used; followed by rapid test and

THANK YOU